REMARKS

Claims 1, 3, 4, 17, 18, and 37 have been amended for clarification, to correct for informalities, or to incorporate elements from a dependent claim. New claim 40 has been added. No new matter has been added. Claims 2, 38 and 39 have been canceled. Upon entry of this amendment, claims 1-37 are present and active in the application.

No new drawings are required since the drawings filed on October 12, 2004, were formal drawings filed in place of informal drawings, having no amendments made to them. Only amended drawings need to bear the label "Replacement Sheet" on them. Applicants maintain that the drawings are in conformance with 37 CFR 1.121(d).

Claims 17, 18, and 37 have been amended for clarification and to correct for informalities. Applicants believe they are now in condition for allowance and request that the objections to these claims be withdrawn.

Claims 38 and 39 have been cancelled and therefore Applicants maintain that there rejections under 35 USC § 101 and 35 USC § 102 should be withdrawn.

REQUEST FOR RECONSIDERATION

The ability to measure the three-dimensional structure of biological tissues is important, but common methods leave out basic information about the molecular composition and metabolic behavior of the tissue imaged. Molecular composition and metabolic behavior information may yield valuable scientific data on the behavior of biological systems, and would be of great clinical diagnostic value for finding diseases, such as cancer. Much of the focus of biological and medical imaging today is to gain information about composition.

Applicants have discovered that nonlinear interferometric vibrational imaging (NIVI) can be used to measure the three-dimensional distribution of molecular species in various samples (biological or otherwise). Its basic operation is to stimulate the excitation of molecular bonds with particular resonance frequencies, and then use these excitations to produce radiation distinct from the excitation (excitation radiation having a different frequency from the stimulating radiation). The physical process of excitation and stimulation of radiation is called Coherent Anti-Stokes Raman Scattering (CARS).

Unlike previous methods that use CARS in microscopy to probe for the presence of molecular species, NIVI utilizes a heterodyne approach where a reference signal is separately generated from a medium, or reference, and interferomerically compared to the signal received from the sample, allowing the signal to be formed into an image in the same way as optical coherence tomography (OCT). In this way, additional information can be inferred from the emitted radiation such as the distance to the sample.

Claim 1 recites a method of examining a sample. The method includes exposing *a reference* to a *first set* of electromagnetic radiation to form a *second set* of electromagnetic radiation scattered from the reference. At least a portion of the second set of electromagnetic radiation is of a frequency *different* from that of the first set of electromagnetic radiation. The reference may be either a sample of a target molecule, a solvent, or a continuum generation medium. (See the specification, page 21, lines 28-29)

The rejection of claims 1-37 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Izatt et al. (U.S. Patent No. 6,002,480) in view of Faris (US 5,451,785) is respectfully traversed. The techniques of the two references are incompatable in that Izatt et al. forms an image from light scattered from a sample, while Faris forms an image from light which is transmitted through a sample.

Izatt et al. discusses a technique for depth-resolved coherent backscatter spectroscopy which is an extension of OCT technology. Izatt et al. also discusses that a conventional scanning Michelson interferometer can be utilized to obtain the depth resolved measurements of reflectors and scatterers in a sample. (Izatt et al., col. 5, lines 53-55). A low coherence light source 10 is separated into two beams by a 50/50 beam splitter 16, fifty percent of the light power is transmitted to a sample arm 12 and the remaining fifty percent is directed to a reference arm 14. (Izatt et al., col. 5, lines 55-59). The reference arm 14 includes a reference probe 22 which transmits the reference beam onto a retroreflecting *mirror* 24, translating towards or away from the reference probe, and collects the light retroreflected back from the *mirror* 24. (Izatt et al., col. 5, lines 62-66). Since a mirror reflects light, there will be no change in

frequency between the electromagnetic energy hitting the mirror 24 and the electromagnetic energy reflected from the mirror 24.

Faris discusses direct two-dimensional transillumination imaging of a sample immersed in or including a scattering medium at infrared to near-infrared wavelengths. (Faris, col. 3, lines 25-28). A radiation source 11 provides a probe radiation beam 12 of a selected frequency generally falling in the infrared or near infrared range. (Faris, col. 4, lines 24-26). An optical arrangement indicated generally at 13 directs radiation beam 12 onto a sample under investigation 14 and spreads the beam to cover a two-dimensional area of the sample. (Faris, col. 4, lines 26-29). The system includes a time-gate subsystem indicated generally at 16 for selecting a temporal portion of beam 12 indicative of photons that are *unscattered or little-scattered by the sample.* (See Faris, col. 4, lines 30-33). To minimize signal loss in the generally low-intensity image-bearing beam from the sample, a mirror 29 is provided which may be formed by a dichroic mirror reflecting the second harmonic reference beam, but not the infrared image-bearing beam which has passed through the sample.

Claim 1 specifies exposing *a reference* to a *first set* of electromagnetic radiation to form a *second set* of electromagnetic radiation *scattered from* the reference, wherein at least a portion of the second set of electromagnetic radiation is of a frequency different from that of the first set of electromagnetic radiation. Izatt et al. uses optical coherence tomography to obtain an image. As a result, light is scattered off a sample and not through it. Since Izatt et al. obtains an image in a completely different way from Faris, by *scattering* light off a sample instead of passing light through the sample, there would be no reason for combining the methods of Faris with the structure shown in Izatt et al. Moreover, the Examiner fails to provide an explanation as to specifically which "methods of Faris" are combinable with the structure of Izatt et al. and fails to provide reasons as why they are combinable.

Moreover, new claim 40 recites exposing a reference to a first set of electromagnetic radiation to form a second set of electromagnetic radiation *inelastically* scattered from the reference. Since a mirror reflects light, and does not scatter the light, there will be no molecular-level interaction between the electromagnetic energy hitting

the mirror 24 and the particles on the surface of the mirror 24, in order to generate light with a different frequency.

Accordingly, Applicants submit that the present invention is neither anticipated by, nor obvious over, Izatt et al. or Faris, either alone or in combination. Withdrawal of this ground of rejection is respectfully requested.

Applicants submit that the application is now condition for allowance. Early notice of such action is earnestly solicited.

Respectfully submitted,

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